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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,513	12/13/2005	Nathalie Marie-Josephe Garcon	VB60298	6380

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
08/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/560,513	GARCON ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-16,18-35,37,39,41-48,51,53-60,62 and 63* is/are pending in the application.

4a) Of the above claim(s) *35,37,39,41-48,51 and 53-59* is/are withdrawn from consideration.

5)☒ Claim(s) *13 and 63* is/are allowed.

6)☒ Claim(s) *12,14-16,18-34,60 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

1. Acknowledgment and entry of the Amendment submitted on 5/11/09 is made. Claims 12-16, 18-34, 60, 62 and 63 are currently under examination. Claims 35, 37, 39, 41-48, 51, and 53-59 were previously withdrawn from consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112-Scope of Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 12, 14-16, 18-34, 60 and 62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising a PRP of H.influenzae B and a polyanionic polymer which is poly-L-glutamic acid (PLG),[wherein PLG reduces the immunological interference that the adjuvant has on PRP or reduces the immunological interference among antigens], does *not* reasonably provide enablement for 'an immunogenic composition comprising a PRP of H.influenzae B and any polyanionic homopolymer wherein the polyanionic polymer is an oligo- or poly-peptide comprising anionic constitutional repeat units selected from the group consisting of L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts thereof; and wherein said oligo- or poly-peptide has a monomer content of no less than 30% L-aspartic acid or L-glutamic acid. '

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification teaches that Applicants have discovered that adding PLG to a vaccine comprising PRP and aluminum hydroxide allows for the PLG to compete with PRP thereby protecting it from any aluminum hydroxide present in the vaccine, e.g., by reducing the amount or rate of binding of PRP to adjuvant and/or the extent or rate of floccuation, yet surprisingly does not cause antigens already absorbed to aluminum hydroxide to become significantly desorbed. The specification also teaches that the PLG provides some protection against immune interference in combination vaccines comprising PRP. However, the results in the instant specification do not demonstrate the use of any other polyanionic polymer which can achieve these results. The instant specification broadly claims an immunogenic composition comprising a PRP of H.influenzae B and ***any*** polyanionic homopolymer which represents an extremely large class of compounds. The specification provides a very large and broad description of what constitutes the invention's 'polyanionic homopolymer' see pages 6-7 of the instant specification. However, the working examples and results have only shown results using PLG (poly-glutamic acid) as the polyanionic homopolymer. The specification teaches that the prior art has taught the use of PLG (poly-glutamic acid) as a drug delivery for cancer therapy and as a biological glue and that the inventors now show its use as an excipient for intramuscular vaccination. It is noted that the instant claims do not require the polyanionic polymer to have all negatively charged repeat units, but

states that the polymer should prevent flocculation between PRP and aluminum hydroxide adjuvant and/or the capability not to significantly desorb antigens beneficially adsorbed to aluminum hydroxide. It would take undue experimentation for one of skill in the art to discover another polyanionic homopolymer from the very large description of the homopolymers which would work in this capacity. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Claim 12 does not even require the polymer to comprise L-glutamic acid, but allows for an oligo- or –polypeptides from any one of L-aspartic acid, D-aspartic acid, L-glutamic D-glutamic acid and salts thereof and no less 30% L-aspartic acid *or* L-glutamic acid. The specification has not shown results with any other composition. It is unclear how may repeat units can be in this oligo- or polypeptide. It would take one of skill in the art undue experimentation to construct a polymer, other than the described PLG, for use in the vaccine/immunogenic compositions as described.

Claim Rejections - 35 USC § 112-written description

4. Claims 12, 14-16, 18-34, 60 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In 1999, the United States Patent and Trademark Office ("USPTO") published training materials regarding the examination of patent applications under the written description requirement of 35 U.S.C. § 112, first paragraph. (See http ://www.uspto. gov/web/offices/pac/writtende sc.pdf). Since that time, the case law and technology have developed in such a way as to necessitate a revision of the 1999 training materials. Consequently, this 2008 revision was created to supersede and replace the 1999 training materials. To the extent that any conflict exists between the 1999 training materials and the present materials, the present materials control. The claims have been evaluated with regard to written description based on the Written Description Guidelines and Training Materials published in 2008/

The instant claims are drawn to 'an immunogenic composition comprising a PRP of H.influenzae B and any polyanionic homopolymer wherein the polyanionic polymer is an oligo- or poly-peptide comprising anionic constitutional repeat units selected from the group consisting of L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid,

and salts thereof; and wherein said oligo- or poly-peptide has a monomer content of no less than 30% L-aspartic acid or L-glutamic acid. '

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. Applicants have not described the genus of polymers such that the specification might reasonably convey to the skilled artisan that Applicants had possession of the claimed invention at the time the application was filed. The Applicants have only shown PLG (poly-L-glutamic acid) and its use for reducing interference between multiple antigens in a PRP combination vaccine composition and for reducing the amount or rate of binding of PRP to adjuvant and/or the extent or rate of floccuation, yet surprisingly does not cause antigens already absorbed to aluminum hydroxide to become significantly desorbed. . The specification provides a very large and broad description of what constitutes the invention's 'polyanionic homopolymer' see pages 6-7 of the instant specification. However, the working examples and results have only shown results using PLG (poly-glutamic acid) as the polyanionic homopolymer. Claim 12 does not even require the polymer to comprise L-glutamic acid, but allows for an oligo- or –polypeptides from any one of L-aspartic acid, D-aspartic acid, L-glutamic

D-glutamic acid and salts thereof and no less 30% L-aspartic acid ***or*** L-glutamic acid. The specification has not shown results with any composition other than PLG. It is unclear how may repeat units can be in this oligo- or polypeptide.

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate

written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed. The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus'" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of variants, the skilled artisan could not immediately recognize that Applicants were in possession of the claimed genus of polymer compositions at the time of filing.

The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification does not describe any members of the claimed genus by complete structure. One of skill in the art would reasonably conclude that the

disclosure fails to provide a representative number of species to describe the genus, and thus, that the applicant was not in possession of the claimed genus. The claimed subject matter is not supported by an adequate written description because a representative number of species has not been described.

There are no drawings or structural formulas disclosed of any of these variants. There is no teaching in the specification regarding how the structure can be varied and still produce a polymer which will have the ability to reducing interference between multiple antigens in a PRP combination vaccine composition and for reducing the amount or rate of binding of PRP to adjuvant and/or the extent or rate of floccuation, yet surprisingly does not cause antigens already absorbed to aluminum hydroxide to become significantly desorbed. Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that the applicant was in possession of the claimed genus of compositions based on disclosure of the single species of only the exact PLG polymer.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to variants/alternatives to PLG 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). With regard to (4) the nature of the invention and (5) the state of the prior art, these have been discussed above. One of skill in the art would require guidance, in order to make or use the compositions as instantly claimed.

Claim Rejections - 35 USC § 112-2nd paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 12, 14-16, 18-34, 60 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The structure of the polyanionic polymer described in claim 12 is vague and confusing and the metes and bounds of what is encompassed by this language cannot be understood. The claim does not even require the polymer to comprise L-glutamic acid, but allows for an oligo- or –polypeptides from any one of L-aspartic acid, D-aspartic acid, L-glutamic D-glutamic acid and salts thereof and no less 30% L-aspartic acid *or* L-glutamic acid. The specification recites the polymer comprises peptide

constitutional repeat units but does not describe any type of limit as to their number or to the different salts thereof or amino acids they may comprise. The polymer as defined is vague and confusing. Appropriate correction is requested..

Allowable Subject Matter

7. Claims 13 and 63 are allowed.

The prior art does not teach or suggest compositions comprising capsular polyribosylribitol phosphate (PRP) polysaccharide of Haemophilus influenzae B and a polyanionic polymer, wherein the polyanionic polymer consists of poly-L-glutamic acid (PLG).

PLGA or DL-PLG microspheres (poly(lactide-co-glycolide) are not the same as the recited PLG (poly-L-glutamic acid). PLGA is not a polyanionic polymer. The instant application provides unexpected results that PLG (poly-L-glutamate) avoids flocculation induced by PRP and that the presence of PLG in Hib formulations reduces immune interference between PRP and Ifanrix-Penta combinations (vaccine comprising multiple antigens).

US Patent No. 6,339,062 mentions PRP and poly-l-glutamic acid in the specification. However, PRP in this application is in reference to Platelet-rich-plasma (PRP), not capsular polyriosylribitol polysaccahride of H.influenzae B.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

8/14/09